CONFIDENTIAL

THE COUNCIL FOR TOBACCO RESEARCH - U.S.A.

February 17, 1966

MEMORANDUM

TO: The committee comprising Dr. Little, Chm., Dr. Andervont and Dr. Reimann.

FROM: Robert C. Hockett

SUBJECT: Interim grant application from Jerome F. Thomas, Ph.D. - No. 535.

We enclose herewith a request from Dr. Jerome F. Thomas of the University of California (Berkeley) , for an interim grant. The attached letter to Dr. Brady explains the situation and the reasons why a short-term grant is needed.

The subject is one relevant to our interests in that we too have been seeking a short-term screening technique for measuring "relative carcinogenicity" of various compounds and mixtures in a semi-quantitative manner. We have explored a number of possible methods and have found most of them unpromising. The one most similar in character to Dr. Thomas's was use of the so-called, photo-dynamic response of Paramecia to polynuclear hydrocarbons. The late Dr. Constantine Stephano attempted to develop this into a rapid and sensitive test on the basis of observations reported by Doniac. Dr. Robert W. Hull, then of the Department of Biological Sciences of Northwestern University, was given a grant (#305) beginning on April 1, 1961, for further refinement, standardization and evaluation of the test. Concurrently Dr. S. S. Epstein of Children's Hospital Medical Center in Boston undertook similar work under other auspices. Dr. Hull made substantial progress over a period of two years. He then transferred to Florida State University in Tallahassee and the second renewal grant was made to that institution as of September 1, 1963. No further reports have been received from Hull since his move.

A part of our original plan was to compare three different bioassay systems with use of the same hydrocarbons, all highly purified, carefully preserved and from the same source. The parallel bioassays were to have been by (1) Dr. B. A. Rubin's method (See grant #181) and (2) an accelerated skin test of Dr. R. K. Boutwell at Wisconsin, with purified hydrocarbons supplied by Dr. Ralph Becker of the University of Houston (#258).

The logistics of the integrated plan broke down mainly because the supply of highly purified hydrocarbons from Becker was inadequate for all three bioassays and Dr. Rubin had first call on the supply. Dr. Boutwell never carried out his part of the plan Rubin and Hull completed their studies independently. (Hull purified his own compounds).

In order to judge the status of our own further interests in this field, we need an up to date report of the state of Hull's work. Dr. Little telephoned him while I was on the way to the west coast. Hull promised to mail us a comprehensive report "next week", but it has not yet been received.

We have also endeavored for some time to interest our grantees in the field of tissue culture to investigate and describe the changes induced by carcinogenic hydrocarbons in cultured cells and endeavor to develop criteria for evaluating the transformation of normal cells to tumor cells. This, we thought, might develop into still another bioassay with some special merits. Dr. Pace (#516) has now finally started such work in the current year. I was not aware of Leo Sachs' papers when I last talked to Pace but will make sure that he is familiar with them.

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MEMORANDUM - Cont'd

In California I talked both to Dr. DeOme and Dr. Thomas. We wanted particularly to learn from the former, who is chairman of the Cancer Research Coordinating Committee of the University, whether Thomas is likely to receive favorable consideration of his project in May. DeOme indicated to me that he is prepared to recommend that his committee renew the grant to Thomas in May provided that he then has a concrete plan to compare his bioassay method with other more conventional ones or with such a method as that of Sachs. (Though he says that some other investigator was unable to confirm Sachs). Of course he does not know for certain whether the rest of the committee will go along with his recommendation.

Dr. Thomas told me that he is much interested in comparing his bacterial method with that of Sachs' and that Dr. Chen is qualified to do so and has actually begun work. The critical problem seems to be Chen's salary from January 1, 1966 until a new university grant is activated, if it is. Thomas would be quite willing to assay fractions of tobacco smoke condensate by his method as a quid pro quo if we provide interim support.

To summarize, Dr. Little and I would hesitate to recommend long-term support to this project unless or until we have fully taken stock of the progress achieved by Hull and by Pace. On the other hand we would look with some favor on a small grant to keep Thomas's staff intact while this evaluation is going on and pending the decision of the university committee as well as to get their comparative observations on some cigarette smoke condensates that have been assayed by our grantees using other methods.

The following papers submitted in support of the application are being sent to the committee only:

1. Manuscript entitled: Photobacterium phosphoreum as an indicator organism for carcinogenic activity. Chi-Sin Chen, and J. F. Thomas.
2. In vitro transformation of normal cells to tumor cells by carcinogenic hydrocarbons. Y. Berwald and Leo Sachs. J. Natl's. Cancer Institute 35, 641 (1965).
3. Inhibition of interferon production in hamster cells transformed in vitro with carcinogenic hydrocarbons. Z. Rotem, Y. Berwald and Leo Sachs. Virology 24, 483 (1964).
4. In vitro cell transformation with chemical carcinogens. Y. Berwald and Leo Sachs. Nature, Dec. 21, 1963, p. 1182.

R. C. H.

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